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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,763	07/19/2004	Gunter Holzemann	MERCK-2903	3011

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	

MAIL DATE	DELIVERY MODE
07/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,763	HOLZEMANN ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2000*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *13,14 and 17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 15-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I claims 1-10, 15-16 and 11-12 drawn to single active ingredient composition with N- [4- (1-benzylpiperidin-4-yloxy)phenyl]-C-phenylmethanesulfonamide as the elected species in the reply filed on May 9, 2007 is acknowledged. The traversal is on the ground that the patent office has not established that it would pose an undue burden to examine the full scope. This is not found persuasive because this application is a 371 case and the restriction was under PCT rule 13.1 for which, at least one Markush alternative is not novel because prior art by Tang et al. CA 133:207639 anticipates group IV thus the lacking of unity of invention has been found.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10, 11-12 being drawn to single active ingredient composition of the compounds, 15-16 are prosecuted. Claims 13-14, 17-20 are withdrawn from consideration per 37 CFR 1.142(b).

2. The claimed benefit for foreign priority cannot be granted at this time since no certified translation was submitted. The effective filing date for the instant application is the PCT filing dated of 17 December ,2002.

3. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what does the scope encompassed by the term "usable derivatives thereof". Although it was described in the specification on pages 4-5 that some examples have been given to the term, but there is no explicit definition for the term. According to the examples, such derivative can include salts or oligopeptides, sugars and polymeric material which are drastically different form salts of small molecule chemical compounds as the claims. Nowhere in the specification provided what salt, what kind of peptide or sugar or polymer would be within the scope of the claims.

4. Claims 1-12, 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description, as well as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention and the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the claims are drawn to all solvates, usable derivatives, mixtures in all ratio for which no description of what kind of solvates, what kind of salts, sugars, etc. such terms is encompassing. None of the examples provided solvates, sugars, etc. In addition, there lacks any description in the structure of formula I, other than the organic nitrogen wherein an acid addition salt can be formed after obtaining the compounds, where a functional group will such broad further derivatization can take place. The further derivatization as generally described encompassed such highly unpredictable field of endeavor (see Braga p. 3640 "*solvate formation can be a nightmare because it isextrely difficult....*"), absent of explicit description with availability of starting material, the specification provided insufficient description and enablement for the claimed scope.

A survey of the specification indicated that the claimed compounds have the expected utility of actions on the central nervous system. The compounds are, in particular, effectors of the nicotinic and/or muscarinic acetylcholine receptor, where they exhibit agonistic or antagonistic action. Nowhere in the specification described or provided any information as to which compound has agonistic or antagonistic, nicotinic or muscarinic acetylcholine receptor, or "effective" against what results. Please note that manipulation of CNS function, especially, acetylcholine transmission system is highly complexed. Not only the drug has to pass the blood brain barrier were the action is in the cerebral system, the binding and quantitative administration of such compounds is highly unpredictable. It is well known that acetylcoline system is where extremely effective poisons such as nerve gases are designed (see Wilbraham p.268-269). Absent of any information on binding efficacy, passing through the blood brain barrier and which receptor site is the specification compound active upon, the specification provided no

information or guidance to one having ordinary skill as to how to pick and choose a compound, how to form a pharmaceutical effective composition, how to operate the "effector" against what.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 11-12, 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baumgarth et al. EP 649,838 supplemented with CA 123:198635 in view of Dougherty et al. US 2004/0180401 (provisional date May 2002).

Determination of the scope and content of the prior art (MPEP §2141.01)

Baumgarth et al. and Dougherty et al. are analogous art in the same field of endeavor of affecting the rhythmic process of the heart. Baumgarth et al. '838 generically disclosed the claimed compounds, see p.3 formula I and provided multiple examples for the generic scope (see CA 123:198635).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art is that instead of identically substituted on the two terminal phenyl rings, the instant claims are drawn to one limited to sulfonamide and the other is other than sulfonamide (see Baugmarth et al. '838, p.3 line 19). Dougherty et al. taught that the same compound as exemplified by Baugmarth has heart rhythm effective activity (see p. 10 right column last compound) and taught that similar compounds having similar activity can be asymmetrically substituted (see page 10 examples).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art is deemed to be aware of all the pertinent art in the field. The above references placed the heart rhythm active compounds in the possession of artisan in the field. The modification of one proven compound with attributes of another proven compound is prima facie obvious. In absence of unexpected results, there is nothing unobvious in choosing some i.e. symmetrically substituted among many i.e. symmetrical as well as unsymmetrical substituted of Baumgarth et al. for the art recognized utility. In re Lemin 141 USPQ 814.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
July 18, 2007

Celia Chang
Primary Examiner
Art Unit 1625